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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/814,891

03/31/2004

Maurice Arthur Trehwella

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BROOKS KUSHMAN P.C.
1000 TOWN CENTER
TWENTY-SECOND FLOOR
SOUTHFIELD, MI 48075

EXAMINER

HA, JULIE

ART UNIT

PAPER NUMBER

1654

NOTIFICATION DATE

DELIVERY MODE

07/09/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Office Action Summary	Application No. 10/814,891	Applicant(s) TREWHELLA ET AL.	
	Examiner JULIE HA	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 April 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 4-34 is/are pending in the application.
- 4a) Of the above claim(s) 16-22,24-30 and 34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-15,23 and 31-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>April 11, 2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Amendment after Non-final rejection filed on April 11, 2008 is acknowledged. Claim 3 has been cancelled. Claims 1-2 and 4-34 are pending in this application. Claims 16-22, 24-30 and 34 remain withdrawn from further consideration as being drawn to nonelected species and invention. Claims 1-2, 4-15, 23 and 31-33 are examined on the merits in this office action.

Withdrawn Rejections

1. Rejection of claims 1-2, 10-11, 13-15 and 31-33 under 35 U.S.C. 112, second paragraph, as being indefinite are hereby withdrawn due to Applicant's amendment.

Maintained Rejection

35 U.S.C. 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-2, 4-15, 23 and 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Kumar et al (Tetrahedron Letters, 1991, 32(16): 1901-1904).
4. The instant claims are drawn to a method of reducing an organic compound (ketone), comprising subjecting the organic compound to a yeast mediated reduction wherein the reduction is conducted in the presence of water and in absence of any

additional solvents. Further, the claims are drawn to the method wherein the compound is precursor for the synthesis of a pharmaceutical Fluoxetine.

5. Kumar et al teach a new chemoenzymatic synthesis of optically pure (R)-Tomoxetine and both the enantiomers of Fluoxetine (see abstract). The reference teaches baker's yeast reduction of ethyl 3-oxo-3-phenylpropanoate (ketone body) to yield ethyl 3-hydroxy-3-phenylpropionate (alcohol), the step comprising Baker's yeast, glucose, and water (see p. 1901, 3rd paragraph and p. 1902, Scheme, step (i)). This reads on claims 1 and 14-15. Since the reference teaches the reduction of starting material (ketone) into the final product (alcohol), the reaction must inherently have all of water-to yeast ratio, temperature conditions, pressure, and must be under the same conditions (i.e., all of reaction conditions including separation steps). Therefore, this reads on claims 2, and 4-13. Further, the reference teaches the synthesis of Fluoxetine (aryl propylamine) (see p. 1902, Scheme, 2a and 2b). This reads on claim 23. Furthermore, it is well known in the art that Fluoxetine (ProzacTM, Eli Lilly Co.) is a potent clinically effective anti-depressant (see p. 1901, 1st paragraph, 2nd sentence). Thus, this reads on claims 31-33.

Response to Applicant's Arguments

6. Applicant argues that "the independent claim 1 is current form recites a method comprising 'subjecting the organic compound to a yeast mediated reduction in the presence of an amount of water that is sufficient for enzymes to be hydrated and but insufficient to provide a visible separate water layer...wherein a water-to-yeast ratio is

up to 1.5 ml/g" Applicant points to "reference five (5) incorporated on page 1901 of Kumar with the reference titled "Asymmetric Reduction of Carbonyl Compounds by yeast II preparation of optically active α - and β -Hydroxy Carboxylic Acid Derivatives' to Deol et al. The Deol describes, Method A.--A thick suspension of industrial yeast (100 g of wet-packed Fermex brand...sucrose (100g) in water (600ml) was prepared and kept at room temperature until vigorous gas production ensued." Applicant argues from the experimental section of Deol cited, it is clear that the water to yeast ratio of 600ml/100g or 6 ml/g is taught and this is far greater than the ratio of up to 1.5 ml/g recited in claim 1. Further, Applicant argues that "by the operation of the invention embraced by the instant claim 1, a yeast mediated reduction is effectuated without laborious after-reaction step for water removal...due to the much simplified process of utilizing a yeast mediated reduction, the method of claim 1 greatly facilitates scale-up applications by reducing reagent consumption and operation costs."

7. Applicant's arguments have been fully considered but have not been found to be persuasive because Kumar reference teaches all of the components of the instant application. As described above, Kumar et al teach the reduction of ketone to an alcohol, as claimed. Since the starting material and the final product are made, it is inherent that the reference's method reaction was under the same reaction conditions as claimed. In regards to the argument that "it is clear that the water to yeast ratio of 6 ml/g is far greater than the ratio of up to 1.5 ml/g recited in claim 1", Applicant is directed to the Kumar reference indicating that "Baker's yeast reduction of 3 yield ethyl 3-hydroxy-3-phenyl propionate (4) has been reported (by Deol) to five not more than 66%

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ee. Using modified conditions we have been able to obtain 4 in 85% ee" (see p. 1901, lines 4-6 of 3rd paragraph). Furthermore, Kumar (in the reference section), indicates that the value reported by Deol was later found to be 54 by Soai et al (see p. 1904, Reference 5). Since the reaction conditions (organic compound, yeast mediated reduction, water, final product) are all met, the reaction must inherently have all of water-to yeast ratio, temperature conditions, pressure, and must be under the same conditions (i.e., all of reaction conditions including separation steps). Further, since Kumar et al indicate that the method of Deol was modified to obtain 4 in 85% ee, the reaction conditions must inherently have all of the same conditions as instant claims. The reference further teaches the final products (R)-Fluoxetine and (S)-Fluoxetine claimed by the instant application. Therefore, the reaction conditions used in the Kumar reference must be the same as the instant application, since water and yeast were used to reduce ketone to alcohol in step (i) to produce the alcohol precursor used to synthesize the final products. In regards to Applicant's argument that "by the operation of the invention embraced by the instant claim 1, a yeast mediated reduction is effectuated without laborious after-reaction step for water removal...due to the much simplified process of utilizing a yeast mediated reduction, the method of claim 1 greatly facilitates scale-up applications by reducing reagent consumption and operation costs" Applicant is reminded that the rejection cited above is an anticipation rejection, not an obviousness rejection. The factors argued were not considered for an anticipation rejection.

Conclusion

8. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). No claims are allowed

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. H./

Examiner, Art Unit 1654

/Anish Gupta/

Primary Examiner, Art Unit 1654